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1: Pflugers Arch 1996 Feb;431(4):571-7.

Natriuretic peptides increase a K+ conductance in rat mesangial cells.

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Mesangial cells (MC) are a main target of natriuretic peptides in the kidney and are thought to play a role in regulating glomerular filtration rate. We examined the influence of cGMP-generating (i.e. guanosine 3',5'-cyclicmonophosphate) peptides on membrane voltages (Vm) of rat MC by using the fast whole-cell patch-clamp technique. The cGMP-generating peptides were tested at maximal concentrations ranging from 140 to 300 nmol/l. Whereas human CNP (C natriuretic peptide), rat guanylin and human uroguanylin had no significant effect on Vm these cells, human BNP (brain natriuretic peptide), rat CDD/ANP-99-126 (cardiodilatin/atrial natriuretic peptide) and rat CDD/ANP-95-126 (urodalatin) hyperpolarized Vm significantly by 1.6 +/- 0.4 mV (BNP, n=8), 3.7 +/- 0.3 mV (CDD/ANP-99-126, n=25) and 2.8 +/- 0.4 mV (urodilatin, n=9), respectively. The half-maximally effective concentration (EC50) for the latter two was around 400 pmol/l each. This hyperpolarization could be mimicked with 0.5 mmol/l 8-bromo-guanosine 3',5'-cyclic monophosphate (8-Br-cGMP) and was blocked by 5 mmol/l Ba2+. The K+ channel blocker 293 B (100 micromol/l) depolarized basal Vm by 4.3 +/- 0.4 mV (n=8), but failed to inhibit the hyperpolarization induced by CDD/ANP-99-126 (160 nmol/l) (n=8). The K+ channel opener cromakalim (10 micromol/l) neither influenced basal Vm nor altered the hyperpolarization induced by 160 nmol/l CDD/ANP-99-126 (n=8). Adenosine (100 micromol/l) hyperpolarized Vm by 13.4 +/- 1.3 mV (n=16). At 100 micromol/l, 293 B did not inhibit the adenosine-induced hyperpolarization (n=6). At 160 nmol/l, CDD/ANP-99-126 enhanced the adenosine-induced hyperpolarization significantly by 1.5 +/- 0.6 mV (n=10). CDD/ANP-99-126 (160 nmol/l) failed to modulate the value to which Vm depolarized in the presence of 1 nmol/l angiotensin II (n=10), but accelerated the repolarization to basal Vm by 49 +/- 20% (n=8). These results indicate that the natriuretic peptides CDD/ANP-99-126, CDD/ANP-95-126 and BNP

hyperpolarize rat MC probably due to an increase of a K+ conductance. This effect modulates the voltage response induced by angiotensin II. The natriuretic-peptide-activated conductance can be blocked by Ba2+, but not by 293 B and cannot be activated by cromakalim. This increase in the K+ conductance seems to be additive to that inducable by adenosine, indicating that different K+ channels are activated by these hormones.

PMID: 8596701 [PubMed - indexed for MEDLINE]
